International Journal of Infectious Diseases (2009) 13, 349—354

http://intl.elsevierhealth.com/journals/ijid

Infectious diseases and the use of antibiotics in outpatients at the emergency department of the University Hospital of León, Nicaragua

C. den Engelsen [a], C. van der Werf [a], A.J. Matute [b], E. Delgado [b], C.A.M. Schurink [a], A.I.M. Hoepelman [a,*]

[a] *Department of Internal Medicine and Infectious Diseases, University Medical Centre, PO Box 85500, F02.126, 3508 GA Utrecht, The Netherlands*
[b] *Department of Medicine, University Hospital, UNAN, León, Nicaragua*

Received 21 February 2008; received in revised form 25 June 2008; accepted 15 July 2008
Corresponding Editor: William Cameron, Ottawa, Canada

KEYWORDS
Infections;
Antibiotics;
Nicaragua;
Resistance;
Guidelines

Summary
Background: In order to develop guidelines for the use of antimicrobial agents, it is necessary to obtain detailed information on the prevalence of infectious diseases and antibiotic usage.
Methods: A retrospective study was conducted among outpatients with acute infections visiting the emergency department of the University Hospital of León, Nicaragua.
Results: Over the course of one month, 2027 patients visited the emergency department. Seven hundred and thirty-two patients (36.1%) had an infection, with a total of 799 acute infections. The majority of patients (55.9%) were children. Respiratory tract infections (43.4%), urogenital infections (29.5%), and diarrhea or gastroenteritis of presumed infectious origin (8.8%) were the most frequent infections. Among respiratory tract infections, the most frequent diagnoses were community-acquired pneumonia (CAP; 31.4%), acute tonsillitis (28.2%), and the common cold (17.6%). CAP was treated with procaine benzylpenicillin in 70.6% of cases, whereas 84.0% of patients with acute tonsillitis were treated with a single dosage of benzathine benzylpenicillin intramuscularly. Among urogenital infections, the most frequent diagnosis was acute uncomplicated urinary tract infection (24.2%). Approximately a quarter of patients with uncomplicated urinary tract infections did not receive treatment according to the local guidelines. Of the patients with acute diarrhea, 27.1% were treated with antibiotics, while only a minority had leukocytes in Wright stain of the feces.
Conclusions: In conclusion our study shows that the use of antimicrobial agents is not optimal. Antibiotics were prescribed too often and not according to the local guidelines. This will further exacerbate the resistance problem in Nicaragua.

* Corresponding author. Tel.: +31 88 75 56228; fax: +31 30 252374.
E-mail address: i.m.hoepelman@umcutrecht.nl (A.I.M. Hoepelman).

1201-9712/$36.00.
doi:10.1016/j.ijid.2008.07.010

Introduction

Resistance to antimicrobial agents is a worldwide problem, leading to higher mortality and greater morbidity. Infections caused by antimicrobial-resistant bacteria lead to an increased length of hospital stay and higher costs.[1–4]

A large percentage of pathogens in developing countries tend to be resistant to the older, inexpensive antimicrobial agents.[5] This could have major negative consequences for individual patients as well as public health, because other antimicrobial agents are often not available. To change this situation, the focus in developing countries should be on increasing the availability of inexpensive, safe, and effective antimicrobial agents and on more responsible drug policies.[6] This is also the case in Nicaragua, a country in which 50% of the population lives in poverty.[7]

Most strategies to reduce resistance to antimicrobial agents involve the development of guidelines for antibiotic use.[8,9] To develop these guidelines, it is first necessary to assess the occurrence of different infections and the use of antibiotics. We have previously studied the etiology and resistance patterns of community-acquired pneumonia (CAP) and urinary tract infections within the University Hospital of León, the second largest city of Nicaragua.[10,11] Based on these data, local guidelines for urinary tract infections were developed.

The purpose of the present study was to obtain detailed information on the prevalence of infectious diseases and the use of antibiotics in the emergency department of the same hospital.

Materials and methods

Study population

A retrospective study was conducted among patients with one or more acute infections, visiting the emergency department of the University Hospital of León, between September 9 and October 18, 2005. This had to be their first emergency department visit with the present infectious episode.

Patients who needed to be admitted to the hospital, patients with more than three acute infections, patients who had more than three antibiotics prescribed, and those cases in which it was unclear which antibiotic was prescribed for which infection, were excluded ($N = 14$).

Definitions

In this study, infections were defined according to the definition given by the clinician. In León, clinicians use the international definitions for CAP and urinary tract infection as stated in our previous publications.[10,11]

Data extraction

Data were collected from medical records. Information obtained included age, gender, and comorbid conditions (asthma, chronic obstructive pulmonary disease, cardiac insufficiency, diabetes mellitus, HIV or other immunocompromising diseases, malignancies, chronic hepatic or renal insufficiency, hypertension, pregnancy, and allergy to antibiotics). The diagnosis was collected and classified according to the ICD-10 classification. The following data were also collected: chest X-ray (presence of infiltrate), leukocyte count in blood (leukopenia: $<4 \times 10^9$/l, leukocytosis: $>10 \times 10^9$/l), presence of bacteria, leukocytes or nitrite in urine, and presence of polymorphonuclear leukocytes in feces after staining with Wright solution.

Data analysis

The statistical analysis was performed with SPSS 12.0.2 for Windows (SPSS Inc., Chicago, IL, USA) software. Only descriptive statistics were used.

Results

Population

During the study period 2027 patients visited the emergency department without being admitted. One hundred and thirty-five patients (6.7%) left before a diagnosis was made; in 162 cases (8.0%) there were insufficient data. Four patients were excluded because more than three antibiotics were prescribed.

Seven hundred and thirty-two patients (36.1%) visited the emergency department because of infections and met the inclusion criteria. Baseline characteristics are shown in Table 1. Figure 1 shows the patients subdivided by age and gender. Most patients were children (55.9% <16 years) and among patients aged ≥16 years the majority were women.

Infections

In the 732 patients included, a total of 799 acute infections were diagnosed. Sixty-three patients had two infections and two patients suffered three infections. Figure 2 shows the distribution of infections according to the ICD-10 classification. The most prevalent were respiratory tract and urogenital infections. Three hundred and forty-seven respiratory tract infections were diagnosed (43.4%). Urogenital infections were diagnosed 236 times (29.5%). The third largest group consisted of diarrhea or gastroenteritis of presumed infectious origin ($N = 70$; 8.8%).

Table 1 Patient characteristics ($N = 732$).

Characteristic	*n* (%)
Age (years), median (range)	11 (0–92)
Children <16 years	409 (55.9)
Women	407 (55.6)
Comorbidities	
Pregnancy	68 (9.3)
Asthma	20 (2.7)
Diabetes mellitus	18 (2.5)
Penicillin allergy	6 (0.8)
COPD	4 (0.5)
Heart failure	3 (0.4)
Renal failure	3 (0.4)
Hypertension	2 (0.3)

COPD, chronic obstructive pulmonary disease.

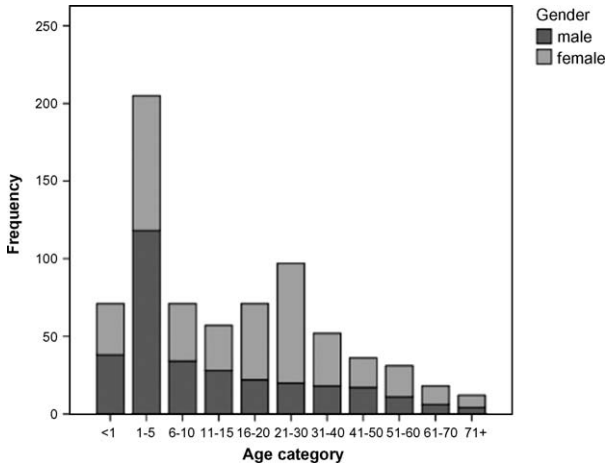

Figure 1 Frequency of the study patients by age and sex.

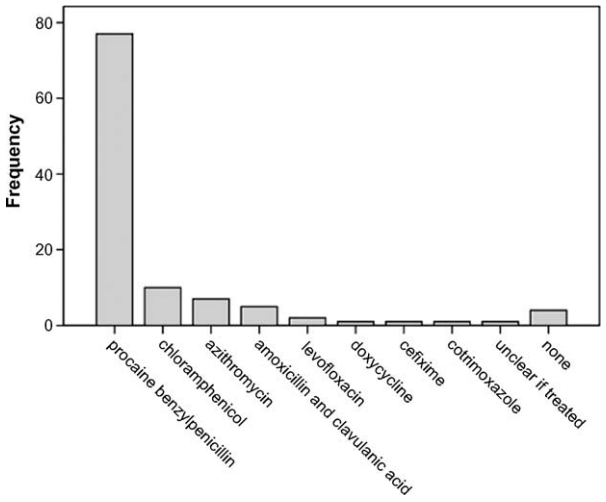

Figure 3 Frequency of prescribed antibiotics for community-acquired pneumonia ($N = 109$).

Respiratory tract infections

Among the respiratory tract infections ($N = 347$), the most frequent diagnoses were CAP (109; 31.4%), acute tonsillitis (98; 28.2%), and common cold (61; 17.6%).

The diagnosis of CAP was made 109 times. Eighty-one patients (74.3%) were under 6 years of age and 70% in this age category were male. Compared to the total study population, more patients with pneumonia had asthma (13.8% vs. 2.7% in the total study population). One hundred and four patients with the diagnosis of pneumonia received antibiotics, four patients did not receive antibiotics, and in one case it was unclear whether the patient received antibiotics. As shown in Figure 3, 77 patients (70.6%) were treated with procaine benzylpenicillin, all intramuscularly. The duration of treatment varied between 5 and 7 days, and dosage was according to body weight. Ten patients (9.2%) received oral chloramphenicol. Adults were treated less often with procaine benzylpenicillin and more often received an oral antibiotic.

The diagnosis of acute tonsillitis was made 98 times. In one case a 'streptococcal tonsillitis' was mentioned, although no throat culture was performed nor was a rapid strep test result available. The other cases were classified as 'acute tonsillitis, unspecified'. Seventy-eight patients (79.6%) were under 12 years of age. The distribution between men and women was equal. Ninety-four patients (95.9%) with acute tonsillitis received antibiotics (Figure 4). Seventy-nine of them (84.0%) were treated with benzathine benzylpenicillin intramuscularly; 22 of these patients received an additional antibiotic (amoxicillin in 16, azithromycin in four, and cefadroxil in two). The treatment with benzathine benzylpenicillin consisted of a single intramuscular dose in all cases; for adults the dosage was 1.2×10^6 units and for children the dosage was adapted to body weight.

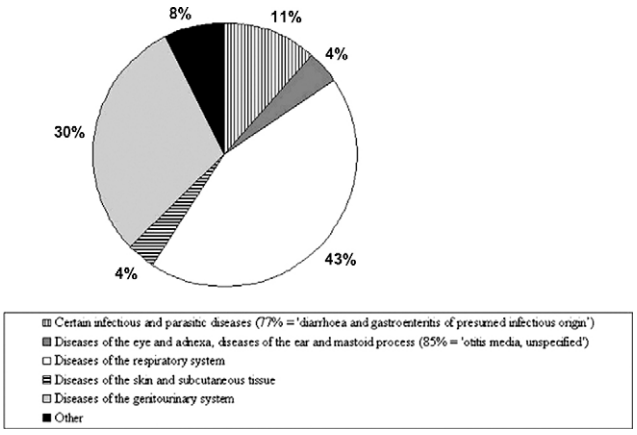

Figure 2 Percentage of most frequently diagnosed infections according to the ICD-10 classification ($N = 799$).

Urinary tract infections

Urinary tract infections were diagnosed 137 times. One infection was defined as cystitis, the other 136 cases were classified as 'urinary tract infections, site not specified'. Most patients were female (106; 77.4%); 24 (22.6%) were pregnant. Half of the patients were aged between 16 and 40 years. Fifty-seven cases (41.6%) were uncomplicated urinary tract infections. Of these patients, 66.7% were treated with ciprofloxacin, 7% with cefalexin, and 7% with amoxicillin.

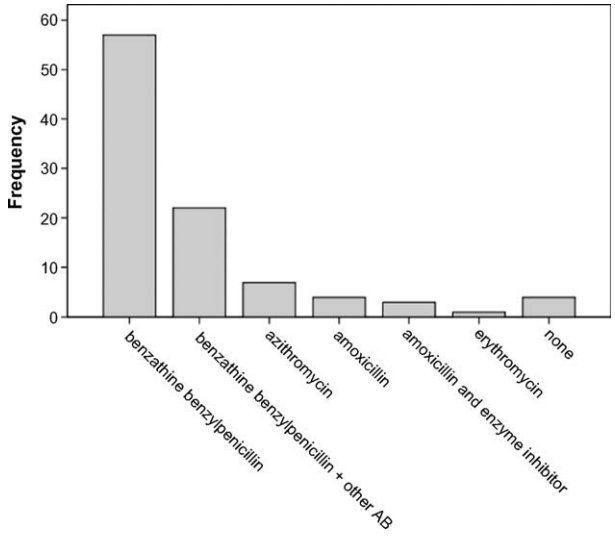

Figure 4 Frequency of prescribed antibiotics for acute tonsillitis ($N = 98$).

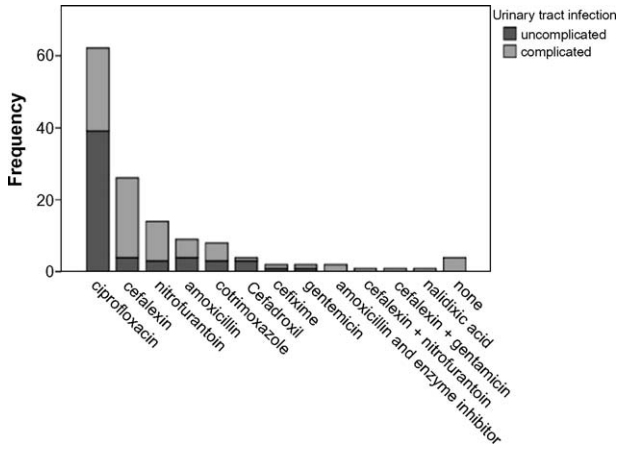

Figure 5 Frequency of prescribed antibiotics for urinary tract infections ($N = 137$).

Cefadroxil, co-trimoxazole, and nitrofurantoin were prescribed each in 5.3% of patients, as shown in Figure 5. Most of the pregnant women received cefalexin (83.3%).

Diarrhea and gastroenteritis

The diagnosis 'diarrhea and gastroenteritis of presumed infectious origin' was made 70 times. Half of these patients were under 6 years of age. In 41 cases (58.6%) a Wright stain was performed on the feces to detect the presence of leukocytes. The results were positive for leukocytes in seven cases; in 15 cases results were not available. In the seven abnormal cases, antibiotics were prescribed three times. Nineteen patients had a normal Wright stain and five of them received antibiotics. No Wright stain was performed for 28 patients; seven of these received antibiotics. Fifty patients (71.4%) did not receive antibiotics and in one case it was unclear whether the patient was treated. Thirteen patients received co-trimoxazole and six patients ciprofloxacin.

Antibiotics in the absence of infection

An antibiotic was prescribed in the absence of an acute infection in 40 cases. These cases varied from prophylactic antibiotics to antibiotics for asthma exacerbations.

Discussion

This is the first study performed to analyze the occurrence of infections and the use of antibiotics at the emergency department of a hospital in Nicaragua. The most prevalent infections were respiratory tract infections, urogenital infections, and diarrhea.

CAP was treated with procaine benzylpenicillin in 70.6% of cases. Matute et al. found in the same hospital in León that 'community-acquired pneumonias' were most frequently caused by *Streptococcus pneumoniae* (17%).[10] This pathogen was sensitive to penicillin in all cases. However, all *Staphylococcus aureus* (5%) were resistant to penicillin. In 55% no pathogen was identified. According to these data, penicillin seems to be an adequate treatment in the majority of cases.

Patients treated with penicillin received this treatment for 5—7 days. A Dutch study, which compared the effectiveness of discontinuing treatment with amoxicillin after three days or after eight days in adults admitted to hospital with mild to moderate/severe CAP, demonstrated that discontinuing amoxicillin after 3 days was not inferior.[12] This suggests that the duration of treatment in Nicaragua could be decreased. However, validated criteria such as the PSI-score or the CURB-65 score should be used to guide the duration of treatment.[13,14]

The majority of cases of acute tonsillitis are of viral etiology. Group A β-hemolytic streptococci are the most common bacterial pathogens. It is usually not possible to distinguish between bacterial and viral pathogens by physical examination. Even when the cause is bacterial, antibiotics are often not necessary. Antibiotics may sometimes decrease the gravity and duration of symptoms, but usually do not benefit the patient.[15] A possible reason for commencing antibiotic treatment, besides a seriously ill patient, is to prevent complications of group A β-hemolytic streptococci such as septic arthritis. In Western countries this is often not necessary, because the incidence of these complications is very low.[16] The incidence in Nicaragua is unknown. However, local clinicians seldom see septic arthritis. In the present study, 96% of patients with acute tonsillitis were treated with antibiotics, which is probably too many.

Matute et al. found *Escherichia coli* to be the pathogen in 56% of positive cultures of urine in patients with urinary tract infection in a former study performed in this hospital.[11] The *E. coli* resistance rate to amoxicillin in León is 74%; for co-trimoxazole this is 63% and for ciprofloxacin 29%. According to the guidelines formulated as a result of this study (Guía terapéutica: infecciones del tracto urinario en adultos, mujeres embarazadas y ninos. HEODRA UNAN León, Nicaragua, 2005, unpublished work), nitrofurantoin, ciprofloxacin, and amoxicillin/clavulanic acid are the first choice antibiotics in uncomplicated urinary tract infections. Approximately a quarter of patients did not receive treatment corresponding to these local guidelines. In these same guidelines, nitrofurantoin, amoxicillin/clavulanic acid, or cefuroxime are recommended for the treatment of pregnant women. Again, the guidelines were not followed precisely in a high number of cases.

In Western countries only a few percent of acute diarrhea cases have a bacterial etiology. In developing countries, this percentage seems to be slightly higher, although rotavirus remains the most frequent pathogen.[17] In a study performed in the suburban area of León, rotavirus was demonstrated in 12.4% of fecal samples from children with diarrhea.[18] The most important bacterial pathogens in Latin America are *E. coli*, *Campylobacter* and *Shigella* species.[19—22] The Infectious Diseases Society of America advises empirical treatment with quinolones in severely ill patients or co-trimoxazole in cases of severely ill children.[19] This can decrease the gravity and duration of infections caused by sensitive *Campylobacter* and *Shigella* species. However, there is a worldwide increasing resistance of *Campylobacter*, *Salmonella*, and *Shigella* species to co-trimoxazole and other antibiotics. This mainly seems to be a problem in developing countries.[19,23] As none of the included patients were admitted into the hospital, one could conclude that these were not severe cases of diarrhea. So, even though the chosen antibiotics are correct according to Western guidelines, it is our opinion that antibiotics are prescribed too often.

The results of Wright stain did not seem to influence policy. However, according to the literature it is a valid tool in diagnosing diarrhea of bacterial origin.[24,25] More consistent use of the results of Wright stain might limit treatment with antibiotics to cases in which the odds of a bacterial pathogen are high.

We registered 40 very diverse cases in which an antibiotic was prescribed in the absence of infection. In some cases there appeared to be an acceptable prophylactic indication. However, in the majority of cases the indication was unclear. In our opinion there is also room for improvement in the use of antibiotics in this area.

The most important potential shortcomings of the present study are due to its retrospective nature, using information from charts. With regard to comorbidities (according to our data comorbidities were present in 119 patients (16.3%), of whom 51 (7.0% of total population) were pregnant), there was probably information missing. In general this is important, as comorbidities in adults can affect the choice of a certain antibiotic. Therefore we recommend that physicians question patients for information on comorbidities and write down this information in the medical records, even if comorbidities are not present. However, given the fact that 56% of patients were children under the age of 16 years, this is probably not of major concern in this study.

In the process of creating guidelines for the treatment of acute infectious diseases, knowledge about the pathogens and their resistance patterns is of great importance. For urinary tract infections and pneumonias in Nicaragua, this has been studied. For gastroenteritis this information is still needed, especially because of the increasing worldwide resistance of bacterial pathogens causing diarrhea to co-trimoxazole, the most frequently prescribed antibiotic in acute diarrhea.

Moreover, the current incidence of group A β-hemolytic streptococci complications should be investigated. With this information, one can consider if it is necessary to treat all cases of acute tonsillitis with penicillin. Group A β-hemolytic Streptococcus rapid diagnostic tests, which have a sensitivity of 80—90% and specificity of 90—100%,[26,27] might be useful to exclude bacterial tonsillitis and reduce antibiotic prescription.

According to the literature, clinical practice guidelines have had limited effect on changing physician behavior.[28,29] Possible factors contributing to this limited effect are lack of awareness, lack of familiarity, lack of agreement, and lack of outcome expectancy.[28] Therefore we recommend that local physicians be instructed on existing guidelines to achieve an actual change in behavior.

In conclusion our study shows that the use of antimicrobial agents in Nicaragua is not optimal. Antibiotics are prescribed too frequently and the spectrum of antibiotics used is too broad. This will exacerbate the resistance problem in Nicaragua. A more structured approach to the diagnosis of infections and a greater awareness of existing guidelines might help in reducing antibiotic usage.

Conflict of interest: No conflict of interest to declare.

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